PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 06050780	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/US06/13551	International filing date *(day/month/year)* 11 April 2006 (11.04.2006)	Priority date *(day/month/year)* 12 April 2005 (12.04.2005)
International Patent Classification (IPC) or national classification and IPC IPC: **A01N 45/00**(2006.01);**A61K 31/56**(2006.01) USPC: 514/171		
Applicant UNIMED PHARMACEUTICALS, INC.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) ____ , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
07 October 2006 (07.10.2006)	29 May 2007 (29.05.2007)
Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer Leonard M. Williams Telephone No. (571) 272-1600

Form PCT/IPEA/409 (cover sheet)(April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US06/13551

Box No. I Basis of the report

1. With regard to the **language**, this report is based on:

☒ the international application in the language in which it was filed.

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))

☐ publication of the international application (under Rule 12.4(a))

☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:
pages 1-29 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☒ the claims:
pages NONE as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* 30-32 received by this Authority on 07 October 2006 (07.10.2006)
pages* NONE received by this Authority on _____

☐ the drawings:
pages NONE as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☒ the claims, Nos. 20
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing (*specify*): _____
☐ any table(s) related to the sequence listing (*specify*): _____

** If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US06/13551

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims 1-19	YES
	Claims NONE	NO
Inventive Step (IS)	Claims 1-19	YES
	Claims NONE	NO
Industrial Applicability (IA)	Claims 1-19	YES
	Claims NONE	NO

2. Citations and Explanations (Rule 70.7)

Claims 1-19 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the use of testosterone in the specifically claimed methods.

Claims 1-19 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

WHAT IS CLAIMED IS:

1. A method of treating, preventing or reducing the risk of developing bone deterioration or osteoporosis in a subject in need thereof, comprising: administering an amount of a hydroalcoholic gel pharmaceutical composition to an area of skin of the subject, which delivers a therapeutically-effective amount of a steroid in the testosterone synthetic pathway to the blood serum of the subject, wherein the composition comprises:

a. about 0.1% to about 10% (w/w) of testosterone or a salt, ester, amide, enantiomer, isomer, tautomer, or derivative thereof;

b. about 0.1% to about 5% (w/w) penetration enhancing agent;

c. about 0.1% to about 5% (w/w) thickening agent;

e. about 45% to about 98% (w/w) lower alcohol; and

f. purified water;

wherein the composition is capable of releasing the steroid after applying the composition to the skin at a rate and duration that delivers at least about 10μg per day of the steroid to the blood serum of the subject; and the percentages are on a weight to weight basis of the composition.

2. The method of claim 1, wherein the steroid in the testosterone synthetic pathway comprises about 1% testosterone, or a salt, ester, amide, enantiomer, isomer, tautomer, or derivative thereof.

3. The method of claim 2, wherein the penetration enhancing agent comprises about 0.1% to about 5% of a C8-C22 fatty acid, a C8-C22 fatty alcohol, a lower alkyl ester of a C8-C22 fatty acid, a di(lower)alkyl ester of a C6-C22 diacid, a monoglyceride of a C8-C22 fatty acid, a tetrahydrofurfuryl alcohol polyethylene glycol ether, a polyethylene glycol, a propylene glycol, a 2-(2-ethoxyethoxy) ethanol, a diethylene glycol monomethyl ether, an

alkylaryl ether of polyethylene oxide, a polyethylene oxide monomethyl ether, a polyethylene oxide dimethyl ether, a dimethyl sulfoxide, a glycerol, an ethyl acetate, an acetoacetic ester, a N-alkylpyrrolidone, a terpene or combinations thereof.

4. The method of claim 3, wherein the penetration enhancing agent is isopropyl myristate.

5. The method of claim 2, wherein the thickening agent comprises about 0.1% to about 5% polyacrylic acid.

6. The method of claim 2, wherein the lower alcohol comprises about 45% to about 90% ethanol or isopropanol.

7. The method of claim 2, wherein the hydroalcoholic gel pharmaceutical composition comprises:

a. about 1 % (w/w) testosterone;

b. about 0.9 % (w/w) CARBOPOL®;

c. about 0.5 % (w/w) isopropyl myristate;

d. about 67 % (w/w) ethanol; and

e. purified water.

8. The method of claim 2, wherein the composition is capable of releasing the testosterone after applying the composition to the skin at a rate and duration that achieves circulating serum concentration of the testosterone greater than about 400ng testosterone per dl serum during a time period beginning about 2 hours after administration and ending about 24 hours after administration.

9. The method of claim 8, wherein the serum testosterone concentration is maintained between about 400 ng testosterone per dl serum to about 1050 ng testosterone per dl serum.

10. The method of claim 2, wherein for each about 0.1 gram per day application of the composition to the skin, an increase of at least about 5 ng/dl in serum testosterone concentration results in the subject.

11. The method of claim 2, wherein the composition is provided to the subject for daily administration in about a 0.1 g to about a 10 g dose.

12. The method of claim 2, wherein the amount of the composition is a 5 g dose delivering about 50 mg of testosterone to the skin.

13. The method of claim 2, wherein the amount of the composition is a 7.5 g dose delivering about 75 mg of testosterone to the skin.

14. The method of claim 2, wherein the amount of the composition is a 10 g dose delivering about 100 mg of testosterone to the skin.

15. The method of claim 2, wherein the composition is provided to the subject in one or more packets.

16. The method of claim 15, wherein the packet comprises a polyethylene liner between the composition and inner surface of the packet.

17. The method of claim 2, wherein the subject has a pretreatment serum testosterone concentration less than about 300 ng/dl.

18. The method of claim 17, wherein after at least about 30 days of daily administration serum testosterone concentration in the subject is at least about 300 ng/dl to about 1050 ng/dl.

19. The method of claim 2, wherein the composition is administered once, twice, r three times daily for at least about 7 days.